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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,257	02/15/2002	Yoram Reiter	02/23338	9820

7590 03/18/2008

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/075,257	REITER, YORAM	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-34* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/534,966.

Claims 1-20 have been canceled.

New claims 21-35 have been added and are currently pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 30, 2007 has been entered.

2. In view of Applicant's amendment filed October 30, 2007 no outstanding ground of rejection is maintained. The following represents a new ground of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 21-27 and 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altman et al (Proc. Nat. Acad. Sci. (USA) [1993] 90:10330-10334; of record) in view of Mottez et al (J. Exp. Med. [1995] 181:493-502; U on form PTO-892, newly cited).

Altman teaches a method for the production of soluble functional MHC class II complexes in *E. coli* (see entire document). Altman teaches the purification of MHC class II from inclusion bodies and the in vitro refolding of the MHC molecules. Altman teaches the association of the MHC molecules with antigenic peptides. Altman teaches that no other proteins are required for the efficient folding of the MHC molecules and that carbohydrate modification is not necessary for T cell recognition. Altman teaches that production in *E. coli* provides large quantities of MHC molecules needed for conformational and functional studies (page 10334 in particular). Altman teaches that production of empty MHC class I

molecules is possible, but is inhibited by the instability of the complex at physiological temperatures (page 10334 in particular).

Altman teaches the purification of complexes including the use of size-exclusion chromatography i (page 10331, column 2 in particular) [claim 22].

Altman teaches denaturation of the inclusion bodies by standard methods (page 10330, column 2 in particular) [claim 26].

Altman teaches reduction of the MHC molecule prior to refolding (page 10331, column 1 in particular) [claim 29].

Altman teaches refolding under renaturation conditions, including oxidized glutathione and arginine (page 10331, column 1 and Figure 1 in particular) [claims 30-34].

Altman does not specifically teach the production of MHC class I molecules or single chain MHC molecules.

Mottez teaches single chain constructs comprising a murine MHC class I heavy chain joined to β_2-microglobulin with a covalently bound antigenic peptide. Mottez teaches that linker, or spacer, sequences separate the segments (see entire document) and allow the proper folding of the MHC class I domains and the peptide. Because the antigenic peptide is attached to the MHC class I molecule, it is constitutively produced in the same cell as the MHC class I molecule [claims 23, 25, 27].

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use the method of Altman to produce the single chain MHC class I molecule of Mottez in *E. coli*. One would have been motivated to combine the teachings with a reasonable expectation of success by the teaching of Altman that MHC molecules do not need accessory molecules for folding and that they do not need glycosylation to be functional. One would have been further motivated by the teaching of Altman that MHC class I molecules are stable at lower temperature, as it is well known in the art that E. coli can be easily cultivated at temperatures at least as low as 4°C. Accordingly, the artisan would have expected to be able to produce large quantities of functional MHC class I molecules at a low cost through use of the combined methods.

3. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Altman et al (Proc. Nat. Acad. Sci. (USA) [1993] 90:10330-10334; of record) in view of Mottez et al (J. Exp. Med. [1995] 181:493-502; U on form PTO-892, newly cited) as applied to claim 21 above, and further in view of Lone et al (J. Immunotherapy [1998] 21(4):283-294; V on form PTO-892; newly cited).

Altman and Mottez have been discussed supra.

Mottez does not specifically teach human MHC class I heavy chain or β_2-microglobulin. However, in a continuation of the same work, Lone teaches that the same techniques were applied to human MHC class I heavy chain HLA-A2.1, which was joined via a 15-amino-acid linker to human β_2-microglobulin. Lone teaches that the single chain MHC class I construct folded properly and was functional (Abstract in particular). Lone teaches that the single chain MHC class I construct specifically bound HLA-A2 restricted peptides and induced peptide-specific cytotoxic T cells to proliferate and produce IL-2.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to substitute human MHC class I as taught by Lone for the murine MHC class I bound to a specific peptide as taught by Mottez. One would have been motivated, with a reasonable expectation of success by the showing of Lone that the human MHC class I complex associated with peptide and activated T cells as well as the murine MHC class I complex did. One would have been further motivated by the teaching of Mottez that single chain MHC class I complexes can be useful for manipulating an immune response, particularly to an antigen that has low affinity for the MHC molecule (page 501, 2nd column in particular).

Conclusion

4. Claim 35 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner
March 11, 2008

/David A Saunders/
Primary Examiner, Art Unit 1644